

Applicants: Jingyue Ju et al.
U.S. Serial No.: 09/823,181
Filed March 30, 2001
Page 12

obviousness of claim 74. Accordingly, applicants request that the Examiner reconsider and withdraw this ground of rejection.

Information Disclosure Statement

In accordance with their duty of disclosure under 37 C.F.R. § 1.56, applicants direct the Examiner's attention to the following references which are listed on the attached Form PTO-1449 (**Exhibit B**) and attached hereto as **Exhibits 1-60**:

- 1) U.S. Patent No. 4,824,775, issued 4/25/89, Dattagupta (Exhibit 1);
- 2) U.S. Patent No. 5,118,605, issued 6/2/1992, Urdea (Exhibit 2);
- 3) U.S. Patent No. 5,302,509, issued 12/4/94, Cheeseman (Exhibit 3);
- 4) U.S. Patent No. 5,654,419, issued 8/5/97, Mathies (Exhibit 4);
- 5) U.S. Patent No. 5,728,528, issued 3/17/1998, Mathies (Exhibit 5);
- 6) U.S. Patent No. 5,770,367, issued 6/23/1998, Southern (Exhibit 6);
- 7) U.S. Patent No. 5,804,386, issued 9/8/98, Ju (Exhibit 7);
- 8) U.S. Patent No. 5,814,454, issued 10/29/98, Ju (Exhibit 8);

Applicants: Jingyue Ju et al.
U.S. Serial No.: 09/823,181
Filed March 30, 2001
Page 13

- 9) U.S. Patent No. 5,834,203, issued 11/10/98, Katzir
(Exhibit 9);
- 10) U.S. Patent No. 5,853,992, issued 12/29/1998, Glazer
(Exhibit 10);
- 11) U.S. Patent No. 5,869,255, issued 2/9/1999, Mathies
(Exhibit 11);
- 12) U.S. Patent No. 5,945,283, issued 8/31/1999, Kwok (Exhibit
12);
- 13) U.S. Patent No. 5,952,180, issued 9/14/1999, Ju (Exhibit
13);
- 14) U.S. Patent No. 6,028,190, issued 2/22/2000, Mathies
(Exhibit 14);
- 15) U.S. Patent No. 6,316,230, issued 11/13/01, Egholm
(Exhibit 15);
- 16) PCT International Publication No. WO 02/079519 A1,
published October 10, 2002 (Exhibit 16);
- 17) PCT International Publication No. WO 02/22883 A1,
published March 21, 2002 (Exhibit 17);
- 18) PCT International Publication No. WO 02/29003, published
April 11, 2002 (Exhibit 18);
- 19) Fei, Z. et al. (1998) MALDI-TOF mass spectrometric typing
of single nucleotide polymorphisms with mass-tagged
ddNTPs. *Nucleic Acids Research* 26(11):2827-2828 (Exhibit

19).

- 20) Olejnik, J. et al (1999) Photocleavable peptide-DNA conjugates: synthesis and applications to DNA analysis using MALDI-MS. *Nucleic Acids Res.* 27(23):4626-4631; (Exhibit 20);
- 21) Axelrod V.D., et al. (1978) Specific termination of RNA polymerase synthesis as a method of RNA and DNA sequencing. *Nucleic Acids Res.* 5(10): 3549-3563 (Exhibit 21);
- 22) Badman, E. R. et al. (2000) A Parallel Miniature Cylindrical Ion Trap Array. *Anal. Chem.* 72:3291-3297 (Exhibit 22);
- 23) Badman, E. R. et al. (2000) Cylindrical Ion Trap Array with Mass Selection by Variation in Trap Dimensions. *Anal. Chem.* 72:5079-5086 (Exhibit 23);
- 24) Benson, S. C., Mathies, R. A. and Glazer, A. N. (1993) Heterodimeric DNA-binding dyes designed for energy transfer: stability and applications of the DNA complexes. *Nucleic Acids Res.* 21: 5720-5726 (Exhibit 24);
- 25) Benson, S. C., Singh, P. and Glazer, A. N. (1993) Heterodimeric DNA-binding dyes designed for energy transfer: synthesis and spectroscopic properties. *Nucleic Acids Res.* 21: 5727-5735 (Exhibit 25);
- 26) Burgess, K. et al. (1997) Photolytic Mass Laddering for Fast Characterization of Oligomers on Single Resin Beads. *J. Org. Chem.* 62:5662-5663 (Exhibit 26);

- 27) Canard B., et al. (1995) Catalytic editing properties of DNA polymerases. *Proc. Natl. Acad. Sci. USA* 92:10859-10863 (Exhibit 27);
- 28) Caruthers M.H. (1985) Gene synthesis machines: DNA chemistry and its uses. *Science* 230: 281-285 (Exhibit 28);
- 29) Chee M., et al. (1996) Accessing genetic information with high-density DNA arrays. *Science* 274: 610-614 (Exhibit 29);
- 30) Chen, X. and Kwok, P.-Y. (1997) Template-directed dye-terminator incorporation (TDI) assay: a homogeneous DNA diagnostic method based on fluorescence resonance energy transfer. *Nucleic Acids Res.* 25: 347-353 (Exhibit 30);
- 31) Edwards, J. et al. (2001) DNA sequencing using biotinylated dideoxynucleotides and mass spectrometry. *Nucleic Acids Res.* 29(21):e104 (Exhibit 31);
- 32) Griffin, T.J. et al. (1999) Direct Genetic Analysis by Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry. *Proc. Nat. Acad. Sci. USA* 96:6301-6306 (Exhibit 32);
- 33) Hacia J.G., Edgemon K., Sun B., Stern D., Fodor S.A., Collins F.S. (1998) Two Color Hybridization Analysis Using High Density Oligonucleotide Arrays and Energy Transfer Dyes. *Nucleic Acids Res.* 26: 3865-6 (Exhibit 33);
- 34) Haff L.A., et al. (1997) Multiplex Genotyping of PCR Products with Mass Tag-Labeled Primers. *Nucleic Acids Res.*

25(18):3749-3750 (Exhibit 34);

- 35) Hyman E.D. (1988) A new method of sequencing DNA. *Analytical Biochemistry* 174: 423-436 (Exhibit 35);
- 36) Ireland R.E., and Varney M.D. (1986) Approach to the total synthesis of chlorothricolide - synthesis of (+/-)-19,20-dihydro-24-O-methylchlorothricolide, methyl-ester, ethyl carbonate. *J. Org. Chem.* 51: 635-648 (Exhibit 36);
- 37) Jiang-Baucom, P. et al. (1997) DNA Typing of Human Leukocyte Antigen Sequence Polymorphisms by Peptide Nucleic Acid Probes and MALDI-TOF Mass Spectrometry. *Anal. Chem.* 69:4894-4896 (Exhibit 37);
- 38) Ju J., Glazer, A.N. and Mathies, R.A. (1996) Energy transfer primers: A new fluorescence labeling paradigm for DNA sequencing and analysis. *Nature Medicine* 2: 246-249 (Exhibit 38);
- 39) Ju J., Ruan C., Fuller, C.W., Glazer, A.N. and Mathies, R.A. (1995) Fluorescence energy transfer dye-labeled primers for DNA sequencing and analysis. *Proc. Natl. Acad. Sci. USA* 92:4347-4351 (Exhibit 39);
- 40) Kamal A., Laxman E., Rao N.V. (1999) A mild and rapid regeneration of alcohols from their allylic ethers by chlorotrimethylsilane/sodium iodide. *Tetrahedron Lett.* 40: 371-372 (Exhibit 40);
- 41) Lee L.G., et al. (1992) DNA sequencing with dye-labeled terminators and T7 DNA polymerase: effect of dyes and dNTPs on incorporation of dye terminators and probability

analysis of termination fragments. *Nucleic Acids Res.* 20: 2471-2483 (Exhibit 41);

- 42) Lee, L.G. et al. (1997) New energy transfer dyes for DNA sequencing. *Nucleic Acids Res.* 25: 2816-2822 (Exhibit 42);
- 43) Li, J., (1999) Single Oligonucleotide Polymorphism Determination Using Primer Extension and Time-of-Flight Mass Spectrometry. *Electrophoresis*, 20:1258-1265 (Exhibit 43);
- 44) Liu, H. et al., (2000) Development of Multichannel Devices with an Array of Electrospray Tips for High-Throughput Mass Spectrometry. *Anal. Chem.* 72:3303-3310 (Exhibit 44);
- 45) Lyamichev, A. et al. (1999) Polymorphism Identification and Quantitative Detection of Genomic DNA by Invasive Cleavage of Oligonucleotide Probes. *Nat. Biotech.* 17:292-296 (Exhibit 45);
- 46) Metzker M.L., et al. (1994) Termination of DNA synthesis by novel 3'-modified deoxyribonucleoside 5'-triphosphates. *Nucleic Acids Res.* 22: 4259-4267 (Exhibit 46);
- 47) Olejnik J., et al. (1995) Photocleavable biotin derivatives: a versatile approach for the isolation of biomolecules. *Proc. Natl. Acad. Sci. USA.* 92: 7590-7594 (Exhibit 47);
- 48) Pelletier H., Sawaya M.R., Kumar A., Wilson S.H., Kraut J. (1994) Structures of ternary complexes of rat DNA polymerase β , a DNA template-primer, and ddCTP. *Science* 264: 1891-1903 (Exhibit 48);

- 49) Prober J.M., Trainor G.L., Dam R.J., Hobbs F.W., Robertson C.W., Zagursky R.J., Cocuzza A.J., Jensen M.A., Baumeister K. (1987) A system for rapid DNA sequencing with fluorescent chain-terminating dideoxynucleotides. *Science* 238: 336-341 (Exhibit 49);
- 50) Ronaghi M., Uhlen M., Nyren P. (1998) A sequencing Method based on real-time pyrophosphate. *Science* 281: 364-365 (Exhibit 50);
- 51) Rosenblum, B.B. et al. (1997) New dye-labeled terminators for improved DNA sequencing patterns. *Nucleic Acids Res.* 25: 4500-4504 (Exhibit 51);
- 52) Ross, P. et al. (1998) High Level Multiplex Genotyping by MALDI-TOF Mass Spectrometry. *Nat. Biotech.* 16:1347-1351 (Exhibit 52);
- 53) Ross, P.L. et al. (1997) Discrimination of Single-Nucleotide Polymorphisms in Human DNA Using Peptide Nucleic Acid Probes Detected by MALDI-TOF Mass Spectrometry. *Anal. Chem.* 69:4197-4202 (Exhibit 53);
- 54) Saxon E. and Bertozzi C.R. (2000) Cell surface engineering by a modified Staudinger reaction. *Science* 287: 2007-2010 (Exhibit 54);
- 55) Schena M., Shalon D., Davis, R. Brown P.O. (1995) Quantitative monitoring of gene expression patterns with a complementary DNA microarray. *Science* 270: 467-470 (Exhibit 55);

- 56) Speicher, M.R., Ballard, S.G. and Ward, D.C. (1996) Karyotyping human chromosomes by combinatorial multi-fluor FISH. *Nature Genetics* 12: 368-375 (Exhibit 56);
- 57) Stoerker J. et al. (2000) Rapid Genotyping by MALDI-monitored nuclease selection from probe libraries. *Nat. Biotech.* 18:1213-1216 (Exhibit 57);
- 58) Welch M.B., Burgess K. (1999) Synthesis of fluorescent, photolabile 3'-O-protected nucleoside triphosphates for the base addition sequencing scheme. *Nucleosides and Nucleotides* 18:197-201 (Exhibit 58);
- 59) Woolley, A. T. et al. (1997) High-Speed DNA Genotyping Using Microfabricated Capillary Array Electrophoresis Chips. *Anal.Chem.* 69:2181-2186 (Exhibit 59); and
- 60) U.S. Serial No. 09/658,077, filed September 11, 2000 (Exhibit 60).

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

Applicants: Jingyue Ju et al.
U.S. Serial No.: 09/823,181
Filed March 30, 2001
Page 20

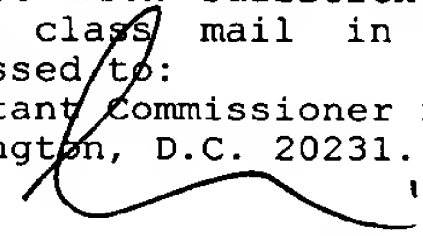
No fee is deemed necessary in connection with the filing of this Amendment. If any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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1/9/03 Date